REMARKS

Applicant respectfully requests reconsideration of this application. Applicant also requests reconsideration of the denial of the request for interference.

Amendments to the claims begin on page 17 of this paper. No new claims are added by this Amendment. The following claims are cancelled by this Amendment: 606, 609, 758, 761, 910, 913, 1050, 1062, 1065, 1201-03, 1205-07, 1211, 1217, 1330, 1333, 1489, 1492, 1617, 1622, 1629, 1630, 1633, 1634, 1648, and 1774.

After this Amendment, the claims pending include: 569-595, 597-605, 607, 608, 610-643, 645-646, 648-651, 654-679, 681-682, 684-687, 690-714, 716-717, 719-747, 749-757, 759, 760, 762-797, 800-803, 806-831, 833-834, 836-839, 842-866, 868-869, 871-899, 901-909, 911, 912, 914-947, 949-950, 952-955, 958-983, 985-986, 988-991, 994-1018, 1020-1021, 1023-1049, 1051, 1053-1061, 1063-1099, 1101-1102, 1104-1107, 1110-1135, 1137-1138, 1140-1143, 1146-1170, 1172, 1173, 1175-1200, 1204, 1208-1210, 1212-1216, 1218-1250, 1252-1253, 1255-1258, 1261-1294, 1296-1329, 1331, 1332, 1334-1407, 1409-1488, 1490, 1491, 1493-1568, 1570-1612 and 1614-1616, 1618-1621, 1623-1628, 1631, 1632, 1635-1647, 1649-1773 and 1775.

All pending claims except claim 1706 were rejected. The majority of the pending claims are amended herein. Some of the amendments correct typos and clerical errors. However, the purpose of most of the amendments is to improve clarity and to remove duplicative terminology, thereby enhancing economy and readability.

I. Objection to Abstract

The Abstract was objected to for exceeding 150 words. On page 16 of this paper is a replacement Abstract that includes less than 150 words.

II. Denial of Request for Interference

A Modified Request for Interference, which will be filed soon, incorporates all claims and amendments entered since the initial Request for Interference was filed on December 21, 2001. The Modified Request also corrects a few errors regarding certain claim designations. For

example, it re-designates certain claims as corresponding to Count 2 rather than to Count 1.[1] Counts 1 and 2 will remain the same.

The denial of interference appears to be based on three grounds. The first ground is that Applicant failed to submit arguments showing that the "non-radioactive label" claimed by Applicant is equivalent to the "chromophore or fluorophore" claimed by Smith in US 5,821,058. The second ground is that the application lacks support for claims reciting "different" indicators. The third ground is that Applicant's claims do not refer to distinguishing nucleic acids based on their "spectral characteristics."

As an initial matter, please note that *an interference may be based on a single allowable application claim* that corresponds to at least one count, even if there are hundreds of other claims in the application that are not allowed or that correspond to no count.[2] Please note also that *the second and third grounds for denial of the interference do not apply to claims that correspond to Count 1*. For example, the term "spectral characteristics" appears only in Count 2. These and other issues are further discussed below.

A. First Ground for Denial of Request for Interference

Again, the first ground for denial is that Applicant failed to submit arguments showing that the "non-radioactive label" claimed by Applicant is equivalent to the "chromophore or fluorophore" claimed by Smith.

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[1] Pursuant to the Modified Request, pending application claims corresponding to Count 1 are: 569-595, 597-605, 607, 608, 610-643, 645-646, 648-651, 654-679, 681-682, 684-687, 690-709, 713, 714, 716-717, 719-747, 749-757, 759, 760, 762-797, 800-803, 806-831, 833-834, 836-839, 842-861, 865, 866, 868-869, 871-899, 901-909, 911, 912, 914-947, 949-950, 952-955, 958-983, 985-986, 988-991, 994-1013, 1018, 1020-1021, 1023-1049, 1051, 1053-1061, 1063-1099, 1101-1102, 1104-1107, 1110-1135, 1137-1138, 1140-1143, 1146-1165, 1169, 1170, 1172, 1173, 1175-1200, 1204, 1208-1210, 1212-1216, 1218-1250, 1252-1253, 1255-1258, 1261-1286, 1290-1294, 1296, 1297, 1700-1704, 1719-1723, 1728-1729, 1732-1740, 1742-1748 and 1766-1768. Pursuant to the Modified Request, pending application claims corresponding to Count 2 are: 710-12, 862-64, 1014-17, 1166-68, 1287-89, 1724, 1741, 1769-1773 and 1775.

[2] "An interference-in-fact exists when **at least one** claim of a party that is designated to correspond to **a** count and at least one claim of an opponent that is designated to correspond to the count define the same patentable invention." 37 CFR 1.610(j). [emphasis added]

(1) Some application claims already recite a fluorophore or chromophore

Both before and after this Amendment, about 120 of Applicant's claims recite a fluorophore or chromophore.[3] Some of these claims recite that the non-radioactive label is fluorescent[4]; others recite that the non-radioactive label is selected from a group that includes fluorescent or chromogenic labels.[5] (A chromogenic label is another word for a chromophore.) Other application claims recite that the non-radioactive label is a specific fluorophore, such as fluorescein, rhodamine or dansyl.[6]

It was error to apply the first ground for denial to the 120 claims that specifically recite a fluorophore or chromophore. All but a handful of these 120 claims correspond solely to Count 1, not Count 2. Because the second and third grounds for denial apply only to claims that correspond to Count 2, and because most of the 120 claims correspond solely to Count 1, the interference should not have been denied for most of these 120 claims.

(2) A generic "non-radioactive label" is patentably indistinct from a generic "chromophore or fluorophore"

With regard to application claims that generically recite a non-radioactive label, Applicant respectfully disagrees with the underlying substance of the first ground for denial. Under 37 CFR §1.601(n), the counts are supposed to be considered prior art to the application claims, and vice versa. The "chromophore or fluorophore" generically recited in the counts would render obvious the application claims that generically recite a non-radioactive label, and

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[3] See claims 638, 640, 642, 660, 661-665, 670, 674, 676, 678, 696-701, 706, 707, 711, 712, 714, 719, 790, 792, 794, 812-18, 822, 826, 828, 830, 848-53, 858, 859, 863, 864, 866, 871, 942, 944, 946, 964-969, 974, 978, 980, 982, 1000-1005, 1010, 1011, 1015, 1016, 1018, 1023, 1094, 1096, 1098, 1116-1121, 1126, 1130, 1132, 1134, 1152-1157, 1163, 1167, 1168, 1170, 1175, 1249, 1267-1273, 1278, 1288, 1289, 1291, 1297, 1728, 1729, 1732, 1739, 1767, 1768, 1769 and 1775.

[4] For example, claims 640, 707, 790, 792, 812-18, 826, 828, 848-53, 859, 863, 864, 942, 944, 1015 and 1767.

[5] For example, claims 719, 794, 822, 830, 858 and 871.

[6] Many previous application claims, including claims originally filed in the parent application, also recited that the non-radioactive label is a generic or specific fluorophore. For example, original claims 28, 42, 43, 87-89 and 130-33, and previous claims 333, 334, 371, 372, 416 and 464-72.

vice versa. Ultimately, non-radioactive detection of nucleic acids nearly always involves detection of color generated by some type of chromophore or fluorophore. At the time of the invention, non-radioactive detection was usually achieved with chromophores or fluorophores that were attached to or that complexed with biotin, avidin or streptavidin. Therefore, it would have been obvious in view of a generic non-radioactive label to use a generic chromophore or fluorophore, and vice versa.[7]

B. Second Ground for Denial of Request for Interference

The second ground for denial is that the application lacks support for claims reciting "different" indicators.

As an initial matter, please note that differential labeling is recited only in Count 2, not in Count 1. Therefore, the second ground for denial does not apply to application claims that correspond only to Count 1.[8]

Applicant also disagrees with the underlying substance of the second ground for denial. Sequencing claims reciting that the indicators are different have been present in the application for at least four years.[9] Until now, there has been no rejection for lack of support for different indicators. Also, in a related application the Examiner allowed claims that recite a "first indicator" and a "second indicator." The related application (App. No. 255,233) is related to the above-captioned application in that the above-captioned application incorporates the actual text of the related application, a continuation of which issued in 1994 to Ward et al as US Pat. No. 5,328,824. Claims 16 and 17 thereof recite the first and second indicators.

There has been no such rejection until now because the above-captioned application contains literal support for using different indicators. It contains literal support in that it

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[7] Fluorophores and chromophores are disclosed throughout the application. *See, e.g.*, Application, pp. 26, 31-37, 47-50, 70, 75, 76, 82, 88, 96 and 102, and original claims 28, 42, 43, 87-89 and 130-33.

[8] Also, in the Modified Request all of the Smith patent claims that recite differential labeling are designated as corresponding to Count 2.

[9] *See, e.g.*, claims 404-406 (added in 1999, now cancelled), and claims 1724 and 1741 (added in 2001).

discloses different non-radioactive indicators, including different fluorescent indicators such as fluorescein, rhodamine and dansyl.[10] The application also discloses using different colored fluorescent indicators to distinguish nucleic acids. For example, the application states:

> By allowing **one set** of labeled clones to hybridize to the chromosomes and then adding a **fluorescent stain** to the label, the set of clones and their locations can be visualized and will **flouresce with a particular color**. A **second set** of labeled clones could then be used and reacted with a **second fluorescent dye**. The same process can be repeated a number of times. Thus one can, if desired, have **several sets of fluorescent labels** attached to the cellular DNA at different but specific locations on each of the chromosomes. . . . [emphasis added][11]

> If necessary, **two sets** of labels can be used – one which would be specific for chromosome 23 and one for some other chromosome. By measuring in each cell the ratio of the two labels, which might be of **different colors**, it is possible to identify the cells which show an abnormal number of chromosomes number 23. This procedure could be used either on slides with a low-light-level video system or in a flow cytometer system using laser excitation. [emphasis added][12]

Although this particular example relates to karyotyping, one of skill in the art would have understood in light of the application as a whole that different fluorophores could equally be used in the sequencing embodiments of the invention.[13] Karyotyping involves detecting specific colors at specific locations on a chromosome. Sequencing involves detecting specific colors at specific locations in a sequencing gel.

C. Third Ground for Denial of Request for Interference

The third ground for denial is that Applicant's claims, unlike certain Smith patent claims, do not refer to distinguishing nucleic acids based on their "spectral characteristics."

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[10] *See* Application, pp. 26, 31, 75, 76, 88 and 96, and original claims 43, 87-89 and 130-33.

[11] Application, p. 47, 1st para.

[12] Application, p.48, 1st para.

[13] *See generally In re Alton*, 76 F.3d 1168, 37 USPQ2d 1578 (Fed. Cir. 1996).

First of all, the term "spectral characteristics" appears only in Count 2, not Count 1. Therefore, the third ground for denial applies only to application claims that correspond to Count 2.[14]

Applicant also disagrees with the underlying substance of the third ground for denial. "Spectral characteristics" are simply characteristics of light emission, such as intensity or color.[15] By definition, different colors inherently have different spectral characteristics. As disclosed in the application, labeled nucleic acids can be detected or distinguished via "colors," "fluorescent illumination," "light microscope visualization," "fluorescent light microscopy," "imaging very low levels of fluorescent light" or "using currently available image intensifiers or systems composed of lasers and photomultipliers."[16] The application also refers, albeit in a somewhat different context, to characterizing nucleic acids "spectrally" or based on "spectral properties," "spectral analysis" and "UV spectra."[17]

Furthermore, the application claims that correspond to Count 2 are directed to a method of sequencing. Distinguishing nucleic acids from one another is the essence of sequencing and therefore inherent in it. The application claims that correspond to Count 2 recite labels that are in fact usually distinguished from one other based on their spectral characteristics. This is particularly true in claims in which the non-radioactive labels are specified as being fluorescent

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[14] Also, in the Modified Request all of the Smith patent claims that include the term "spectral characteristics" are designated as corresponding to Count 2.

[15] A "spectral characteristic" is "The relation between wavelength and some other variable, such as between wavelength and emitted radiant power...." *McGraw-Hill Dictionary of Scientific and Technical Terms*, 5th Ed. (1994). Wavelength is another word for color. Color is defined as "A general term that refers to the wavelength composition of light...." *Id.*

[16] *See* Application, p. 32, 2nd para. ("fluorescent illumination"), p. 36, 3rd para. ("colored precipitates permits light microscope visualization," "fluorescent light microscopy"), p. 37, 2nd para. ("Detecting and/or imaging very low levels of fluorescent light is possible using currently available image intensifiers or systems composed of lasers and photomultipliers....Using systems of this kind or flow systems in which the cells or parts of cells flow past a laser beam, one can obtain sensitivity increases for fluorescent material....This increase is sufficient to detect the fluorescence of single copy genes."), p. 47, 1st para. (reproduced in Section B above), p. 48, 1st para. (reproduced in Section B above).

[17] *See* Application, pp. 40-46.

or chromogenic or in which the labeled fragments are detected by means of a fluorescent or chromogenic measurement.

As shown below, Smith et al discussed related issues during prosecution of the Smith patent. *Smith et al's discussions are relevant to interpretation of Count 2 because Count 2 is identical to claim 41 of the Smith patent.*

> [T]he tags are spectrally distinguishable, that is, the basis for detection of nucleotides in any given sequence undergoing analysis.[18]
>
> As previously pointed out, the tagged compositions of the invention are **inherently detectable**. That is, no additional chemical reactions are necessary for detection of the tagged compositions of the invention. An oligonucleotide labeled with a chromophore is detectable simply by virtue of its color (i.e., light absorption), which emission from a fluorophore-labeled oligonucleotide is detectable upon illumination with light having a wavelength appropriate for the particular fluorophore. One exemplary advantage of the inherent detectability of the claimed compositions is that they can be detected while undergoing electrophoretic separation and other types of biochemical manipulations. This property of the claimed compositions allows, for example, rapid DNA sequence analysis in real time. . . . [emphasis in original][19]

The examiner in the Smith prosecution agreed that detecting a fluorophore and observing its spectral characteristics are one and the same. For example, in an Office Action in the Smith prosecution, the examiner wrote: "...detect the fluorescence (i.e., 'spectral characteristics') of the label."[20]

Furthermore, Count 2 does not require that labeled nucleic acids from all four of the sequencing reactions be distinguishable from each other. Only "one" must be distinguishable. Smith reiterated this point during prosecution:

> Since there are four different nucleotides present to be detected, the **"classical" case** to which the present invention applies **involves the use of four tags, each being distinguishable from the others** by its spectral characteristics. **However**

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[18] Amendment, mailed November 13, 1990, and Amendment, mailed October 14, 1991, Appl. No.: 106,232

[19] Amendment dated February 26, 1999, Appl. No.: 08/484,340

[20] Office Action dated April 13, 1994, Appl. No.: 07/898,019

> **this is not to say that the invention including the claims must be limited to the "classical" case. It is clear that one may use the present invention and detect just the one type (out of the four)** nucleotide present in the oligonucleotide being sequenced. . . . The claims should not be restricted to the "classical" case which is but the most complete and elaborate application of this invention. . . . [21]
>
> The enablement provided by the Specification is **not limited to the "classical" case**, and is enabling for the detection of just the one type (out of the four) nucleotide present in the oligonucleotide being sequenced. The advantages of the present invention obtain in such a process just as they do in the "classical" case, and is equally enabling for the simpler case which is but a subset of the "classical" case. . . .The Specification is admitted sufficient for the "classical" case, and is equally enabling for the simpler case which is but a subset of the "classical" case. [22]

For the reasons above, Applicant respectfully requests reconsideration of the Denial of the Request for Interference.

III. Written Description Rejections

The Office Action rejects various claims as insufficiently described. Specifically, the Office Action alleges that the application lacks written support for certain linkages of the Sig moiety to the sugar or phosphate. With regard to various other claims,[23] the Office Action alleges lack of support for using indicator molecules that are the same or different.

Please note that most of the claims for which Applicant has requested an interference are not subject to these rejections.[24]

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[21] Amendment, mailed November 13, 1990, and Amendment, mailed October 14, 1991, Appl. No.: 106,232

[22] Amendment mailed September 10, 1992, Appl. No.: 07/660,160; Amendment mailed October 14, 1991, Appl. No.: 07/558,312

[23] Claims 1475, 1477-1581, 1709, 1723-1726, 1740, 1741, 1758 and 1759.

[24] With regard to claims that correspond to Count 1, claims 569-616, 621, 624-709, 713-768, 773, 776-861, 865-920, 925, 928-1013, 1018-1072, 1077, 1080-1165, 1169-1223, 1226, 1227, 1230-1234, 1239, 1242-1286, 1290-1297, 1700-1704, 1719-1722, 1728-1729, 1732-1739, 1742-1748 and 1766-1768 are not subject to this rejection. With regard to claims that correspond to

A. Attachment of Sig

The current and previous Office Actions rejected claims for specifically reciting that the Sig of any of the nucleotide structures (i)[25], (ii)[26] or (iii)[27] can be attached via an amine linkage, glycosidic linkage or olefinic bond.

Applicant respectfully traverses the rejection. However, in an effort to move prosecution forward, Applicant has amended the claims to satisfy the Examiner's concerns. Attachment of Sig via an amine linkage, glycosidic linkage or olefinic bond is now recited explicitly only for the Sig of nucleotide structure (i).

B. Different or Same Indicators

The Office Action states that certain claims[28] "contain limitations to the practice of different or same indicator molecules," but the application does not support multiple indicators "which are either of a 'different' or 'same' type."

With regard to "different" indicators, Applicant respectfully traverses the rejection for the reasons set forth above in Section II(B) and II(C) of this paper.

With regard to "same" type indicators, Applicant respectfully traverses the rejection for the following two reasons.[29] First, to say that the application lacks support for "different" type indicators implies that the application at least has inherent support for "same" type indicators. Both grounds of rejection cannot be advanced simultaneously. Second, most of the examples disclosed in the application employ *one* type of indicator, *i.e.*, the *same* type of indicator. Therefore, there is at least implicit support for same type indicators throughout the application.

Count 2, claims 710-12, 862-64, 1014-17, 1166-68, 1287-89 and 1769-1775 are not subject to this rejection.

[25] Sig is attached to the base.

[26] Sig is attached to the sugar.

[27] Sig is attached to the phosphate.

[28] Claims 1475, 1477-1581, 1709, 1723-1726, 1740, 1741, 1758 and 1759.

[29] Claims that are directed only to same type indicators, and not to different type indicators, include claims 1573, 1577, 1723, 1725, 1740 and 1758.

IV. Enablement Rejection

The Office Action asserts that the term "sugar" is not fully enabled. For the reasons set forth in Applicant's previous responses, Applicant respectfully disagrees. However, to minimize further delay, Applicant has now amended the claims to satisfy the Examiner. Throughout the claims, the term "sugar" has been changed to "furanose."

V. Indefiniteness Rejections

The Office Action alleges that the terms "indicator molecule," "indicator molecules" and "compound" cause confusion. In the currently amended claims, these terms have been changed, respectively, to "indicator moiety," "indicator moieties" and "structure."

The Office Action also alleges that the metes and bounds of the claimed "analogs" are indefinite. For the reasons set forth in Applicant's previous responses, Applicant respectfully disagrees. However, to minimize further delay, Applicant has now amended the claims to satisfy the Examiner. Specifically, throughout the claims Applicant has removed nearly all recitation of "analog" or "analogs." As such, none of the claims recite "base analog," "sugar analog," "phosphate analog," "pyrimidine analog," "purine analog," "deazapurine analog," and the like.

In some of the claims, Applicant retained the term "nucleotide analog." The metes and bounds of the nucleotide analog are expressly defined in these claims. For example, in amended claim 569, the nucleotide analog: (1) must be capable of being incorporated within, or onto a terminus of, the nucleic acid fragment, (2) must not substantially interfere with the ability of nucleic acid fragment to hybridize to the nucleic acid of interest, *and* (3) must be non-radioactively modified or non-radioactively labeled on its "furanose moiety," "phosphate moiety" or "base moiety." The nucleotide analog is further defined tacitly by the inherent requirement that it be useful in the claimed "process for determining the sequence of a nucleic acid of interest." In other words, the nucleotide analog cannot have features that are inconsistent with this process or its component steps.

The Office Action also alleges that various claim terms and phrases appear to lack antecedent basis or otherwise cause confusion. Applicant has revised or replaced the offending

terms and phrases. For example, the Office Action alleges that claim 1411 is indefinite because it is unclear "whether a non-radioactively labeled protein may also be radioactively labeled even though it is detected via its non-radioactive characteristics." Applicant has now amended claim 1411 to clarify that the protein is non-radioactive as well as non-radioactively detectable. Similarly, claims 1177 and 1704 previously recited the phrase "modified or labeled non-disruptively or disruptively on at least one of..." Applicant has changed this phrase to "non-radioactively modified or non-radioactively labeled, non-disruptively or disruptively, on at least one of..."

VI. Prior Art Rejections

A. Kourilsky et al

The Office Action rejects various claims under 35 USC 102(e)(2) in view of Kourilsky et al.

Applicant has now amended these claims to recite that the second segment of the polynucleotide is an "operator sequence" for which the non-radioactively detectable protein must have a binding affinity. In a telephone conversation between Applicant and the Examiner on May 7, 2003, the Examiner appeared to agree that this particular amendment overcomes Kourilsky et al.

B. Dunn et al

The Office Action rejects various claims under 35 USC 102(b) in view of Dunn et al. The Office Action takes the position that Dunn's ligation of a polynucleotide tail (SV40) to a polynucleotide probe (Ad2) anticipates Applicant's claimed process for preparing a detectable non-radioactively labeled polynucleotide. In other words, the Office Action essentially alleges that the nucleotide structure (iii) of the rejected claims – in which Sig is attached to the phosphate – is anticipated by two polynucleotides connected via the normal phosphate linkage, as long as one of the two connected polynucleotides can be detected without using radioactivity.

Applicant respectfully disagrees with the rejection. First, UV absorbance could *not* have been used to detect Dunn's Ad2/SV40 probe. In a liquid phase system, UV absorbance can be

used to detect nucleic acids by passing light through a cuvette and then measuring the amount of light that proceeds through the other side. In Dunn, the nucleic acids are bound to a nitrocellulose filter. UV absorbance cannot be used with nitrocellulose filters because they do not allow the UV light to pass through.

Second, Applicant is unaware of what other system could have been used to detect the unmodified Ad2/SV40 probe hybridized to the adeno target in the absence of hybridization with a probe labeled with ^{32}P or non-isotopic labels such as biotin or fluorescein. Applicant is unaware of a system that could distinguish between a signal generated by the target adeno DNA on the filter and a signal generated by a target adeno plus a small amount of hybridized AD/SV40 RNA probe without using 32P or non-isotopic labels such as biotin or fluoroscein. Nor could the method of Dunn have been adapted to a liquid phase hybridization. UV absorption could be carried out in such a liquid phase, but the hybridization of the Ad2/SV40 probe would not be distinguished from complementary adeno target strands that renature.

Third, the labeled polynucleotide of Applicant's claimed process can be detected non-radioactively because of the presence of a signalling moiety. The term 'moiety' typically refers to a *component* of a molecule that is structurally different in kind from the rest of the molecule. Although the Sig of Applicant's claims encompasses polynucleotides, those polynucleotides must themselves include a signalling moiety structure that is itself non-radioactively detectable.

The requirement of a distinct signalling moiety is now clearer because, in nucleotide structure (iii) of independent claim 1582, Applicant has added the word "signalling" in front of the word "moiety." Also, amended claim 1582 now specifies that the non-radioactive detection is due to "an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, an electron density measurement, a magnetic measurement, or any combination of the foregoing measurements."

Furthermore, amended claim 1582 now recites that the signalling moiety "is detected" non-radioactively. Dunn does not disclose actual non-radioactive detection of the SV40 tail. Therefore, the SV40 tail of Dunn is irrelevant regardless of whether it is "capable" of being detected non-radioactively.

Applicant has also amended the claims depending from claim 1582 that refer to nucleotide structure (i) or (ii). It is now clear in these dependent claims that the nucleotide structure is limited to nucleotide structure (i) or (ii), and that nucleotide structure (iii) is excluded from these dependent claims.

C. Langer et al or Dale et al

The Office Action rejects various claims under 35 USC 103(a) in view of Langer et al or Dale et al.

These claims have been amended to recite that the second segment of the polynucleotide is an "operator sequence" for which the non-radioactively detectable protein has a binding affinity. In a telephone conversation between Applicant and the Examiner on May 7, 2003, the Examiner appeared to agree that this particular amendment overcomes Langer et al and Dale et al as well as Kourilsky et al.

D. Hartman et al

The Office Action rejects various claims under 35 USC 103(a) in view of Hartman et al.

The rejected claims have been amended to recite that Sig comprises at least three carbons. The alleged equivalent of Sig in Hartman et al – the azido group – contains only one carbon. Nothing with three carbons attaches to or replaces the azido group. The azido group merely catalyzes the polymerization of methacrylate. Methacrylate has at least three carbons, but it does not attach to or replace the azido group of Hartman et al. Indeed, the methacrylate never attaches to any nucleotide or polynucleotide in Hartman.